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Characteristics of intermittent and persistent allergic rhinitis: DREAMS study group

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Summary

Background In the Allergic Rhinitis and its Impact on Asthma (ARIA) classification, intermittent and persistent rhinitis were proposed to replace seasonal and perennial allergic rhinitis (AR).

Aim To better understand the ARIA classification of rhinitis.

Methods A cross-sectional study was carried out in 591 patients consulting ENT or allergy specialists for AR and 502 control subjects. The diagnosis of AR was based on a score for allergic rhinitis (SFAR) ≥ 7. Patients were classified according to the four ARIA classes (mild intermittent, mild persistent, moderate/severe intermittent and moderate/severe persistent). Allergen sensitization (skin prick tests (SPTs) or specific IgE) and co-morbidities were examined according to the ARIA classes.

Results Ten percent of patients had mild intermittent rhinitis, 14% mild persistent rhinitis, 17% moderate/severe intermittent rhinitis and 59% moderate/severe persistent rhinitis. Most patients with intermittent rhinitis had a pollen sensitivity, but 5% had a single house dust mite (HDM) sensitization. Over 50% of patients with persistent rhinitis were allergic to pollens or HDM. Asthma was present in 24% of rhinitis patients and in only 2% of the control population ($P<0.0001$). Patients with moderate/severe persistent rhinitis had the highest asthma prevalence (33%).

Discussion Intermittent and persistent rhinitis are not synonymous of seasonal and perennial rhinitis. Most patients consulting specialists have severe rhinitis. Asthma prevalence increases with duration and severity of rhinitis supporting the ARIA major recommendation that patients with persistent rhinitis should be evaluated for asthma.

Keywords allergy, ARIA, asthma, rhinitis

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Introduction

The recent Allergic Rhinitis and its Impact on Asthma (ARIA) recommendations have proposed a new classification for allergic rhinitis (AR) [1–3]. Previously, AR was subdivided, based on the time of allergen exposure, into seasonal, perennial and occupational diseases [4–6]. However, this subdivision is not entirely satisfactory as: (1) it is often difficult to differentiate between seasonal and perennial symptoms, (2) the exposure to some pollen allergens is long standing [7–9], (3) nasal inflammation is prolonged for weeks after pollen exposure in patients with seasonal rhinitis [10], (4) the exposure to some perennial allergens is not similar over the year [11, 12] and symptoms may be of short duration, and (5) the majority of patients are polysensitized to pollen and perennial allergens [13, 14].

In the ARIA classification, intermittent and persistent rhinitis were proposed to replace seasonal and perennial AR. In a large population of over 6000 patients, it was shown that around 55% of patients with seasonal symptoms had an intermittent rhinitis whereas 55% of those sensitized to perennial allergens had persistent rhinitis [15] showing that the terms seasonal and perennial are not synonymous of intermittent and persistent. However, more information is needed to appreciate the characteristics of patients with intermittent and persistent rhinitis.

A cross-sectional study was carried out in 591 patients consulting ENT or allergy specialists for AR and 502 control subjects. Patients were classified according to the four classes of ARIA (mild intermittent, mild persistent, moderate/severe intermittent and moderate/severe persistent) using the ARIA classification [1]. The characteristics of rhinitis, allergen sensitization and co-morbidities were examined according to the ARIA classes.

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Methods

Subjects

All patients with AR were recruited in ENT or allergist offices and fulfilled the following inclusion criteria: (1) Patients of

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Table 1. Components of the SFAR

Nasal symptoms in the past year including sneezing, runny nose and blocked nose when the subject did not have a cold or the 'flu' in the past year
Nasal symptoms accompanied by itchy-watery eyes (rhinoconjunctivitis)
Season of the year in which nasal symptoms occur (from which two variables were defined: seasonal and perennial rhinitis, respectively)
Triggers of nasal symptoms including pollens, house dust mites, house dust and epithelia
Perceived allergic status
Previous medical diagnosis of allergy
Previous positive tests of allergy
Familial history of allergy

SFAR, score for allergic rhinitis.

both genders ranging in age from 18 to 50 years had a history of AR during at least the past 2 years (10; 5–15 years). (2) All had an AR and the diagnosis of AR was based on a score for allergic rhinitis (SFAR) $\geqslant 7$ [16]. We decided to use the SFAR (Table 1) in order to have a homogeneous diagnosis of AR in the patients and controls as SFAR$\geqslant 7$ allows satisfactory discrimination between subjects with and without rhinitis [16]. (3) Allergic sensitization was assessed using skin prick tests (SPTs) with standardized allergens (Stallergènes, Anthony or Allerbio, Varenne en Argonne, France) and/or serum-specific IgE (CAP System, Pharmacia Diganostics, Uppsala, Sweden). In the present study 69% of the patients had SPTs and 37% had serum-specific IgE. The following allergens were tested: grass pollen, tree pollen, *Dermatophagoides pteronyssinus*, cat dander, *Alternaria* and *Cladosporium*. In areas where ragweed is prevalent, allergen sensitivity to this allergen was also tested. Monosensitization was defined as sensitization to one allergen. Trees pollinate in France up to the end of April. Thus, differentiation is not needed and we did not make any differentiation in the questionnaire between pollen species. Moreover, although there is no epidemiologic study available in France, clinically, there are two mite seasons, one around May and the second after the end of August.

The control group of 502 individuals without AR was defined according to the SFAR (SFAR score <7), which is highly specific for AR. The control group was issued from the general population. No diagnosis of specific allergy was made in this group. It was chosen to have a similar age and sex distribution of the DREAMS population.

Subjects were enrolled from May to September 2002 in order to cover pollen and house dust mite (HDM) seasons. The study was done in all regions of France to rule out any geographic or seasonal parameter.

Classification of rhinitis and diagnosis of co-morbidities

Patients were categorized as having intermittent or persistent rhinitis according to the ARIA classification [1]. Patients with skin tests/IgE to pollens without any other sensitivity were classified as 'seasonal', whereas patients with mite and/or multiple sensitivities were classified as 'perennial'. There were very few patients with pollen and animal sensitivities ($N = 18$, 3, 1%) or pollen and mould sensitivities ($N = 8$, 1, 4%).

Conjunctivitis was defined clinically according to the single question used in the ISAAC and the SFAR questionnaires [16] on suggestive symptoms: 'In the past 12 months, has the nose problem been accompanied by itchy-watery eyes ?' The question 'Diagnosed asthma' was used to assess asthma.

Statistical analysis

All clinical variables were summarized by descriptive statistics. Qualitative data are presented as frequencies and quantitative data as medians and 25–75 percentiles.

A generalized linear model was used to study the effects of the type of AR, the severity of rhinitis and their association as independent variables.

For the description of quantitative variables, the Kruskall–Wallis test with Bonferroni–Dunn's *post hoc* analysis was used. The χ^2 test was used for qualitative variables.

Statistical analyses of the collected data were performed using SAS software, version 8 (SAS Institute, Cary, NC, USA). For the description of the studied populations, descriptive statistics are provided. Normality of data was assessed using the Shapiro–Wilk test and statistical analysis was made using parametric tests.

Results

Demographic characteristics of the patients

In the present study 828 patients were included, but only 591 patients were analysed. The reasons for exclusion were deviations from the protocol: age ($N = 123$), SFAR<7 ($N = 230$), not measurable ARIA classes ($N = 7$). The demographic characteristics of the patients are presented in Table 2. The only difference between cases and controls was the employment status with a lower percentage of workers among the cases.

Eighty five percent of the patients were treated for their nasal conditions whereas only 3% of the subjects in the control group had such a treatment. Oral H1 antihistamines were administered in 77% of the patients and 64% of them had an intra-nasal corticosteroid. There was no difference in the medical treatment of patients with intermittent and persistent rhinitis.

Table 2. Demographic characteristics of the patients

	Cases, $n = 591$	Controls, $n = 502$	*P*-value
Gender, *n* (%)			NS
Females	313 (53)	264 (53)	
Males	278 (47)	238 (48)	
Age in years, mean (SD)	34 (9)	34 (9)	NS
Employment status, *n* (%)			<0.0001*
Farmer	10 (2)	4 (1)	
Craftsman, shopkeeper	41 (7)	13 (3)	
Manual worker	29 (5)	115 (23)	
Executive, intellectual, employee	358 (61)	256 (51)	
Unemployed	149 (25)	115 (23)	
Residence, *n* (%)			NS
Cities and towns	426 (74)	393 (78)	
Villages	151 (26)	109 (22)	

P-value by χ^2 test except for age.
*Significance related to all the status of employment.
SD, standard deviation; NS, non-significant.

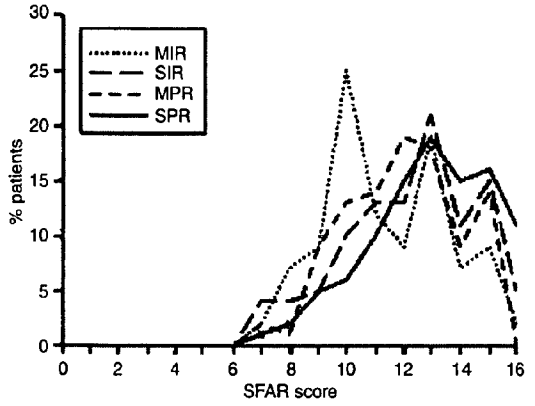

Fig. 1. Score for allergic rhinitis (SFAR) score depending on the allergic rhinitis and its impact on asthma classes.

Repartition of patients in the four Allergic Rhinitis and its Impact on Asthma classes

Mild intermittent rhinitis was diagnosed in 10% of patients, mild persistent rhinitis in 14%, moderate/severe intermittent rhinitis in 17% and moderate/severe persistent rhinitis in 59%.

The SFAR scores were studied in the four ARIA classes (Fig. 1). There was a significant difference between the severity of rhinitis (mild vs. moderate/severe, $P=0.015$) and the type of rhinitis (intermittent vs. persistent, $P<0.001$) but there was no interaction between these two parameters.

Co-morbidities Asthma was present in 24% of AR patients whereas it was only present in 2% of the controls (Fig. 2) ($P<0.0001$, χ^2 test). The prevalence of asthma was associated with the duration (intermittent vs. persistent, $P<0.05$) and severity of rhinitis (mild vs. moderate/severe, $P<0.05$).

The prevalence of conjunctivitis was similar in patients with intermittent (64%) and persistent rhinitis (66%).

Allergenic sensitivity

Monosensitization (skin and/or IgE tests) to pollen was significantly more frequent in intermittent rhinitis than in the persistent form ($P<0.0001$; Fig. 2). Monosensitization to dust mites (skin and/or IgE tests) was significantly more frequent in persistent rhinitis than in the intermittent form ($P<0.0001$). However, 8% of the patients with intermittent rhinitis were only sensitized to mites and 21% of the patients with persistent rhinitis were only sensitized to pollens.

Pollen sensitization was observed in 87% of patients with intermittent rhinitis and, 72% of patients with persistent rhinitis (NS). There was no significant difference between them. Mite sensitization was found in 35% of patients with intermittent rhinitis and 72% of patients with persistent rhinitis ($P<0.0001$) (Fig. 3).

Patients with mite allergy had less often moderate/severe rhinorrhea than those with pollen allergy (Table 3). They also had less often intermittent rhinitis than the persistent one. Patients with pollen allergy had more often conjunctivitis and less often asthma.

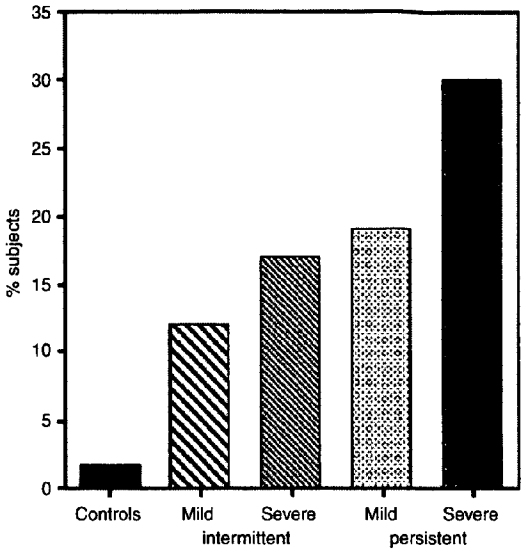

Fig. 2. Monosensitization to pollen and house dust mites depending to the allergic rhinitis and its impact on asthma (ARIA) classes $P<0.0001$ for the effect of ARIA classes on positivity prevalence intermittent vs. persistent: 15.4% vs. 27.6% ($P=0.01$); mild vs. severe : 16.3% vs. 26.9% ($P=0.04$).

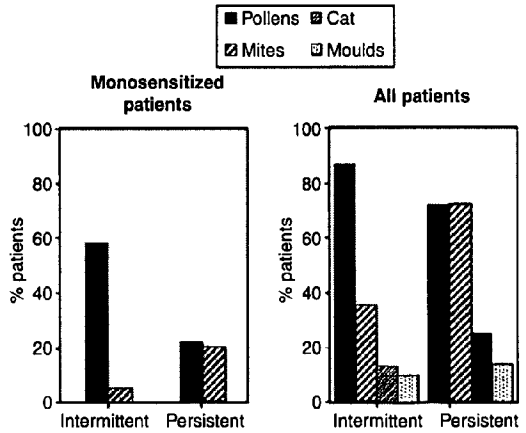

Fig. 3. Positivity of allergic tests (skin prick tests and/or serum-specific IgE) in patients with intermittent and persistent rhinitis (allergic rhinitis and its impact on asthma (ARIA) classification) $P<0.05$ for the effect of ARIA classes on positivity prevalence mite intermittent: 35% vs. mite persistent: 72% ($P<0.0001$); pollen intermittent: 87% vs. pollen persistent: 72% (NS).

Discussion

In this study carried out in specialist practices on a large number of patients with AR, it was found that 76% of the subjects had moderate/severe rhinitis according to the ARIA classification. Although most patients with intermittent rhinitis had a pollen sensitivity, the same is true for persistent rhinitis. On the other hand, HDM allergy is more common in persistent that in intermittent rhinitis. Many patients allergic to pollen only had persistent rhinitis. The prevalence of asthma was low in non-rhinitis subjects and significantly

Table 3. Symptoms of patients depending on their allergenic sensitivity

	Mite allergy (%)	Pollen allergy (%)	Mite and pollen allergy (%)	*P*-value
Symptoms of rhinitis				
Moderate/severe rhinorrhea	67	80	77	<0.02
Moderate/severe nasal obstruction	91	84	84	NS
Moderate/severe sneezing	68	60	65	NS
Moderate/severe nasal pruritus	41	55	49	<0.02
ARIA classes				<0.01
Intermittent rhinitis	12.2	42	12.8	
Persistent rhinitis	87.8	58	87.2	
Conjunctivitis	58	81	71	<0.01
Asthma	35	23	34	<0.04

P value by χ^2 test.
ARIA, allergic rhinitis and its impact on asthma.

increased in patients with rhinitis. Those with moderate/severe persistent rhinitis had the highest prevalence.

All subjects were included over the pollen and mite seasons to overcome the possible seasonal differences in symptoms and reporting. However, as many patients were included during the spring pollen season, there may be an over-representation of pollen-allergic patients. This indicates that this study cannot be used as an epidemiologic study to assess the prevalence of allergenic sensitization.

The diagnosis of AR was based on a score, the SFAR which has been validated to accurately diagnose patients with AR [16]. It was therefore used in both the group of patients and the control group. However, a few patients with AR are not diagnosed using the SFAR and it may be argued that those diagnosed have a more severe disease. We, however, decided to use a score as, in the validation of the ISAAC questionnaire on AR [17], it was found that the ISAAC core questions on rhinitis are highly specific and therefore useful in excluding atopy, but they have a lower sensitivity for detecting atopy in a general population of children. Similar observations have been made in adults [18]. Other scores may have been used, but the SFAR was selected as it was validated in French.

The diagnosis of allergy is sometimes difficult and SPTs and/or serum-specific IgE have been used. As it has been shown that IgE and SPTs have an equal efficiency [19, 20], both tests can be used equally. We did not perform intradermal skin tests as they were shown to add little to the diagnostic evaluation [21].

The classification of the duration of rhinitis symptoms was made according to ARIA [1]. Confirming the study of Demoly et al. [15] this study showed that seasonal and perennial rhinitis are not synonymous of intermittent and persistent rhinitis. In this study around 50% of the patients were seen by ENT/allergologist and 50% by Gps. The results were comparable between the two physician's groups. Pollen allergy was present in 87% and 72% of patients with intermittent and persistent rhinitis. Thirteen percent of patients with intermittent rhinitis were allergic to HDMs. Most patients were polysensitized. Thus, it appears that the ARIA classification appears to be more appropriate than the older one as it confirms the reasons explaining why the classification had to be changed.

In this study, most patients presented moderate/severe symptoms and persistent rhinitis is more common than intermittent. The selection of the treated patients in specialist offices using a score is likely to increase the prevalence of severe persistent patients. However, in another study carried out in 3052 patients (53% treated) studied in primary care (J. Bousquet et al., unpublished data), similar percentages of patients with severe (intermittent and persistent) rhinitis were found. These results suggest that when patients consult for AR they usually suffer from severe and/or persistent symptoms. A study in the general population is, however, needed to assess the prevalence of the four classes of AR, especially in patients who are not consulting physicians.

The prevalence of asthma was very low in the controls and these results are in accordance with the data of Pariente et al. [22] and Leynaert et al. [23]. In this study carried out in the patients of the European Community Respiratory Health Survey, 1.5% of the subjects without AR by questionnaire had a diagnosis of asthma. Twenty four percent of the patients with rhinitis suffered from asthma. These results are also consistent with previous data in the general population. In the present study, it was found that the severity and duration of rhinitis were associated with asthma prevalence. This is in accordance with the studies of Leynaert et al. [23, 24] in which, among patients with AR, those with seasonal and perennial allergy have the highest prevalence of bronchial hyper-reactivity and diagnosed asthma. These results confirm the major recommendation of ARIA stating that patients with AR should be tested for asthma [1].

The prevalence of conjunctivitis is high in both patients with intermittent and persistent asthma. These results were expected as it has been widely published that patients with AR often have ocular symptoms.

Exposed to a common environment, only certain individuals develop an IgE-mediated immune response and this differs from subject to subject, some of them reacting towards a limited number of allergens whereas others are sensitized to a wide array of allergens. Pepys [25, 26] categorized atopic status into 0, 1, 2 or 3 or more groups according to the number of positive SPTs to a small battery of relevant allergens (e.g. grass or ragweed pollen, HDMs, cat and a locally important mould allergen). Taking into consideration cross-reactivities between allergens and panallergens, a minority of symptomatic patients is sensitized to a single allergen (monosensitized) whereas over 75% present IgE antibodies against several allergens (polysensitized) [13]. Mono- and polysensitized patients are different in terms of immune response [27–30]. In the present study, we found that pollen monosensitization was more common in patients with intermittent rhinitis, but we also found that patients with persistent rhinitis could have a mite or pollen monosensitization.

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